Remarks

Claims 1-43, 72-75, 83-91, and 133-141 are pending. Claims 44-71, 76-82 and 92-132 have been withdrawn from consideration. As discussed in the telephone interview of April 14, 2006, claims 1 and 72 have been amended to include functional limitations for HEX-α and HEX-β. Support for this amendment can be found at least in the paragraph bridging pages 14 and 15. Also as discussed in the telephone interview, claims 12 and 16 have been amended and claims 142 and 143 have been added to recite specific percent homologies. Support for new claims 142 and 143 can be found at least in original claims 12 and 73. Applicant believes that the amendments herein do not constitute new matter or raise new issues. Depending on the actions of the Examiner with respect to the new and amended claims, the Applicant may want to amend the claims such that allowed claims reciting specific percent homologies are made independent and new claims identical to those of claims 2-11 and 13-19 are made dependent thereon.

Summary of Interview

Applicant would like to thank Examiner Hama for her comments during the telephone interview of June 29, 2006 to discuss the Advisory Action mailed June 8, 2006. The Examiner indicated that the Amendment filed May 26, 2006 was not entered on the basis that the functional limitation added to claim 1 was considered to require a new search. The Examiner also indicated that reference to the ability of HEX-α and HEX-β to form a dimer would require a teaching of the specific dimerization domains. The Applicant pointed out that dimerization could be easily detected and that prediction was not required. However, in response to the Final Office Action dated January 27, 2006, the Applicant has amended claims 1 and 72 to include the catabolic activity as the only functional limitation.

Applicant would also like to thank Examiner Hama for her helpful comments during the telephone interview of April 14, 2006. Regarding the withdrawal of the rejection over whether or not the orientation of the two cistrons relative to the IRES were enabled in light of *in vitro* uses, the Examiner confirmed that this withdrawal was not an indication that *in vivo* uses were not enabled or that the claims should be limited to *in vitro* uses.

Regarding the enablement and written description rejection of claims 1-43, 72-75, 83-91, and 133-141, the Examiner indicated that the Applicant should include a functional limitation into the claims such that an artisan can know whether a mutant form of HEX-α or HEX-β can be used in the claimed compositions and methods. The Applicant has amended the claims accordingly.

The Examiner also stated that she would again review the evidence provided by the Applicant that at 70% homology, most protein mutants will have the essential physical properties of an identified protein (Tian, W. and Skolnick, J. J Mol Biol. 2003 Oct 31;333(4):863-82, another copy of which is attached hereto as Exhibit A). The Applicant has amended the claims to separately recite 95%, 85%, and 70% sequence identities in order to facilitate prosecution and allowance. However, Applicant's arguments for the allowance for claims directed to HEX proteins which are at least 70% homologous are provided herein.

I. Double Patenting

Applicant acknowledges and appreciates the withdrawal of the rejection of claims 1-43, 72-75, and 83-86 under 35 U.S.C. § 101 for statutory type double patenting.

II. Rejection under 35 U.S.C. § 101

Applicant acknowledges and appreciates the withdrawal of the rejection of claims 1-43, 84-91, and 133-141 under 35 U.S.C. § 101.

III. Rejection under 35 U.S.C. § 112, first paragraph - Enablement

Claims 1-43, 72-75, 83-91, and 133-141 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. Applicant acknowledges and appreciates the withdrawal of the rejection relative to IRES orientation, HEX delivery, promoters, and vectors.

A. Structure and Function

The rejection is maintained for allegedly failing to identify what regions of SEQ ID NO:1 and SEQ ID NO:3 need to be conserved in order for the claimed invention to work. In order to facilitate prosecution, the Applicant has amended claims 1 and 72 to recite the functional limitation "wherein the HEX-α and HEX–β can catabolize GM_2 ganglioside." Support for this amendment can be found at least in the paragraph bridging pages 14 and 15. One of skill in the art would be able to combine the disclosed structural (i.e., sequence) and the corresponding functional (GM_2 catabolysis) characteristics of HEXA and HEXB to ascertain whether a given HEX mutant can be used in the present invention.

B. Percent Homology

As to the Applicant's position that the claimed invention is enabled for HEX proteins which are 70-95% identical to SEQ ID NO:1 or SEQ ID NO:3, the Examiner has stated that "[w]hile it may be true that there are some examples wherein a molecule with 70% or greater homology to a known sequence will have essential physical properties of the identified structure, the problem here is that nothing in the specification or the art provide guidance as to what regions of SEQ ID NO:1 and SEQ ID NO:3 need to be conserved in order for the claimed invention to work" (emphasis added).

However, as demonstrated in the article provided in the Applicant's response on November 9, 2005, most (~90%) mutants will maintain enzyme function with sequence identities as low as 60%, and in fact enzyme function does not generally *start* to diverge until the sequence identity is below 70% (Tian, W. and Skolnick, J. J Mol Biol. 2003 Oct 31;333(4):863-82, attached herewith). This indicates that nearly 100% of proteins with 95% or greater, 85% or greater, and even 70% or greater identity retain enzymatic activity. The Examiner indicated in the telephone interview of April 14, 2006 that she would re-examine the claims based on this evidence.

Thus, the Applicant would expect, with a very high level of certainty, that any given sequence would function. Further, as discussed extensively throughout the present application,

certain mutations are well known to cause neurodegenerative diseases. Thus, if one factors in the knowledge of amino acids that are important for function to the analysis, the skilled artisan would likely never pick a sequence that would not function.

Further, while the skilled artisan has a high expectation that any given sequence having 70% identity would function, if needed, it is routine experimentation for one skilled in the art to test such variants to determine if they fit into the claimed homology and to assay said variant for functionality (e.g., GM_2 catabolysis).

Accordingly, the Applicant respectfully requests the withdrawal of the rejection, and allowance of claims 1-43, 72-75, 83-91, 133-141, and new claims 142 and 143.

IV. Rejection under 35 U.S.C. § 112, first paragraph - Written Description

Claims 1-43, 72-75, 83-91, and 133-141 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement.

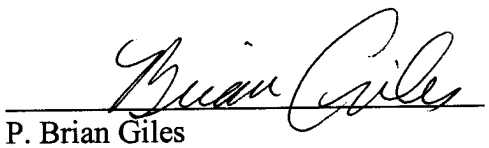
Applicant acknowledges and appreciates the withdrawal of the rejection relative to IRES orientation and promoters.

The Examiner has maintained the rejection relative to HEX-α and HEX–β mutants, stating that "[t]he issue at hand is that nothing in the art or specification provides structural and corresponding functional characteristics of HEXA and HEXB protein such that an artisan can obtain mutants of HEXA and HEXB and know whether or not they have activity." In order to facilitate prosecution, the Applicant has amended claim 1 and 72 to recite the functional limitation "wherein the HEX-α and HEX–β can form a HEXA heterodimer, and wherein the HEXA can catabolize GM_2 ganglioside." The Applicant believes that this limitation, combined with the above evidence that most mutant forms of HEX-α and HEX–β will be functional with as little as 70% homology, is sufficient to overcome this rejection.

Accordingly, the Applicant respectfully requests the withdrawal of the rejection, and allowance of claims 1-43, 72-75, 83-91, 133-141, and new claims 142 and 143.

A Request for Continued Examination (RCE) and a Request for a Three Month Extension of Time is enclosed. A Credit Card Payment authorizing payment in the amount of $845.00, representing $395.00 for the RCE fee required under 37 C.F.R. § 1.17(e) and $450.00 for the fee under 37 C.F.R. § 1.17(a)(3) ($510.00 for the three-month extension of time minus $60.00 for the one-month extension of time fee filed on May 26, 2006 was made electronically. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No.14-0629.

Respectfully submitted,
NEEDLE & ROSENBERG, P.C.



P. Brian Giles
Registration No. 57,896

NEEDLE & ROSENBERG, P.C.
Customer Number 23859
(678) 420-9300
(678) 420-9301 (fax)